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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/241,595	02/02/1999	JORG REIMANN	9325-0008.30	8928

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/241,595	REIMANN ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11 and 13-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-11 and 13-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response received on 11/5/03 has been entered. New claims 32-35 have been added. Claims 1, 3-11, and 13-35 are pending in the instant application. An action on the merits follows.

The text of those sections of Title 35, US code, not included in this office action can be found in the previous action, paper no. 6.

Claim Rejections - 35 USC § 112

The rejection of original, amended or new claims 1, 3-11, and 13-35 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained. Applicant's arguments have been fully considered but have not been considered persuasive in overcoming the following instant grounds of rejection for reasons of record as discussed in detail below.

As noted in the previous office action, a single issue remains in this scope of enablement rejection. The prior office actions have stated that the ability to generate CTL *in vivo* is significantly affected by the antigen and route of administration. Specifically, the previous office actions stated that genetics, dose or concentration of antigen, and route of antigen administration contribute to the unpredictability of generating CTL, helper T cell, and/or B cell responses in vivo (Abbas et al. and Golding et al).

The applicants argue that the claims have been amended to recite wherein the HBsAg compositions are administered to the subject, "by injection into the body of said subject" and that the crux of the applicant's invention does not lie in the route of administration but rather on the inherent ability of the HBsAg particles to enhance CTL responses.

In response, the amendments to the claims are very broad and read on the use of numerous routes of delivery including intravenous, intraperitoneal, subcutaneous, and intramuscular. The previous office actions have pointed out that while the specification and declaratory evidence have provided data demonstrating the induction of CTL responses to HBsAg particles comprising various cytokines, ODNs, and/or peptide antigens, none of these experiments disclose or provide guidance as to the route of administration. As such the specification fails to provide sufficient guidance to overcome the unpredictability associated with various routes of delivery of antigen and the generation of immune responses. As noted above, the previous office actions have provided evidence that genetics, dose or concentration of antigen, and route of antigen administration contribute to the unpredictability of generating CTL, helper T cell, and/or B cell responses in vivo (Abbas et al. and Golding et al). Therefore, applicant's arguments in the absence of supporting evidence are not sufficient to overcome the evidence of record relating to the unpredictability of generating CTL responses using different routes of administration of the HBsAg/antigen particles.

Applicant's amendments to the claims have resulted in the following new grounds of rejection.

Claims 1, 3-11, 13-26, and 31-35 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendments to independent claims 1, 11, 17, and 31 have introduced a new limitation which is not supported by the specification as filed. The claims now recite wherein the biologically active molecule is not covalently modified. The specification as originally filed does not support this limitation. Therefore, this new limitation is new matter. The applicants have pointed to page 7, lines 24-25 for support for this limitation. However, on page 7, lines 24-25, the specification states, "The present compositions in contrast, are prepared by simple incubation of the components, not involving covalent modification.". The "components" referred to are HBsAg and a biologically active molecule. The sentence is describing how the compositions are made, thus "not involving covalent modification" is referring to combining the biologically active molecule and HBsAg. The meaning of this sentence is clear when read in the context of the previous paragraph. The previous paragraph on page 7, lines 12-23, describes compositions known in the prior art comprising HBsAg-antigen fusion proteins made by either covalently linking the HBsAg and antigenic peptides or by expressing the fusion protein from chimeric DNA constructs. Thus, in lines 24-25, the applicants are differentiating their own invention which does not require the covalent attachment of the antigen to HBsAg from the prior art. This limitation, "wherein the biologically active molecule is not . covalently attached to said HBsAg particle" was previously added to the claims by amendment and is supported by this disclosure on page 7, lines 24-25. The specification does not disclose that the biologically active

molecule cannot be covalently modified, it simply discloses that the biologically active molecule cannot be covalently attached to HBsAg. Therefore, the specification as filed fails to provide adequate written description for the newly added negative limitation which would limit to the invention to biologically active molecules which have not undergone any covalent limitation.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is claimed. (See Vas-Cath at page 1117). Furthermore, adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. As discussed in detail above, the specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 28 and 30 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 28 recites the limitation "said incubating step" in claim 27, and claim 30 recites the limitation "said incorporating step" in claim 29. There is insufficient antecedent basis for these limitations in claims 27 and 29 respectively. Specifically, neither claim 27 nor claim 29 recites a "step". Claim 27 recites, "comprising

incubating said particle", and claim 29 recites, "comprising incorporating a glycolipid". Thus, there is no antecedent basis for a "step" in these claims.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 5-6, 11, 17-18, 25-27, and 29-30 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,039,522 (8/13/91), hereafter referred to as Neurath, is withdrawn over claims 1, 5-6, 11, 17-18, and 25-26 and maintained over claims 27, and 29-30. Applicant's amendments to claims 1, 11, and 17 has overcome this rejection, however please note that these amendments have resulted in new grounds of rejection of these claims under 35 U.S.C. 112, first paragraph, for new matter, see above. Applicant's arguments as they apply to claims 27, and 29-30 have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the claims have been amended to recite that the antigenic molecules are not covalently modified, whereas Neurath et al. discloses that the antigen is covalently bonded to a myristal group. In response, claims 27, and 29-30 have not been amended to recite the limitation that the biologically active molecule is not covalently modified. Thus, this argument is not compelling.

The applicant further argues that the present invention is directed to enhancing a CTL response, whereas Neurath et al. teaches enhancing antibody responses. In response, claims 27, and 29-30 are methods of incorporating a biologically active molecule into an HBsAg particle

and do not recite any limitations as to the use of those particles. The only method steps recited involve incubating the HBsAg particle in the presence of the biologically active molecule. Thus, applicant's arguments relating to the intended use of the compositions resulting from the claimed method are not compelling.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's

supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER